intravaginal pentamycin for the treatment of bacterial vaginosis

C. Winnips[1,*], J.A. Balmer[2]

[1] *Lumavita AG, Basel, Switzerland*
[2] *Gynäkologie und Geburtshilfe, Spiez, Switzerland*

Background: Pentamycin 3 mg vaginal tablets (FemiFect®, Lumavita AG, Basel, Switzerland) is effective in the treatment of vaginal infections caused by *Trichomonas vaginalis*, *Candida albicans* and mixed flora (Clin. Ter. 92: 137-142, 1980; Internet Journal of Gynecology and Obstetrics 11(1), 2009). While pentamycin has shown in-vitro activity against some pathogenic bacteria, it is inactive against the lactobacilli that colonize the healthy vagina, making it an ideal therapeutic candidate for the treatment of bacterial vaginoses. The objective of this study was to investigate the efficacy, safety and tolerability of intravaginal pentamycin in women with symptomatic bacterial vaginosis.

Methods: This open-label clinical trial included 92 women, aged 15-78 years, who attended the gynaecology clinic for symptoms of vaginitis and had a diagnosis of bacterial vaginosis on the basis of the history, complete gynaecological examination, wet mount evaluation and microbiological analysis. The causative agent was primarily *Gardnerella vaginalis* in 43 patients, while diverse bacteria were found in the vaginal secretions of the other 49 women.

Twenty-five patients had previously received other antimicrobial therapies without benefit. Patients were treated with intravaginal pentamycin (6 mg daily for 5 days, n = 58; 3 mg daily for up to 10 days, n = 34), either alone (73.9% of cases) or in combination with other therapies. The gynaecological examination and microbiological analysis were repeated at the end of the treatment period, when the occurrence of systemic or local adverse events was also recorded and patient's satisfaction was assessed by using a questionnaire. Efficacy endpoints were resolution of symptoms and eradication of the causative agents.

Results: Resolution of symptoms and eradication of the causative agents were demonstrated in 74.4% and 69.8%, respectively, of patients with bacterial vaginoses primarily caused by *G. vaginalis* and in 87.8% and 75.5%, respectively, of patients with bacterial vaginoses caused by diverse bacteria. Irrespective of the dose of pentamycin administered, treatment acceptance was rated as ''good'' by 69.8% of patients with bacterial vaginoses primarily sustained by *G. vaginalis* and 79.6% of those with a disease caused by diverse bacteria. The therapeutic regimen was well-tolerated in all cases.

Conclusion: Intravaginal pentamycin, either alone or in combination with other therapies, is effective in the treatment of bacterial vaginoses. The drug exhibits a favourable tolerability profile and is well-accepted by patients.

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intravenous colistin therapy for infections caused by multidrug-resistant gram-negative bacteria in critically ill patients

M. Cusato

Fondazione IRCCS Policlinico San Matteo, Pavia, Italy

Background: The increasing incidence of infections caused by multidrug-resistant (MDR) *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and *Klebsiella pneumoniae* is a worldwide problem, particularly among patients with immune deficiency, burns or neutropenia. The significant resistance of these bacteria to the commonly used antibiotics and the expected lack of new agents available in the near future lead the clinicians to test the efficacy and safety of colistin, an old antibiotic whose use decreased because of suspected toxicity and which is now used as the last therapeutic resort.

Methods: Thirteen (10 M, 3F; mean [SD] age 45.3 [18.3] years; mean [SD] estimated body weight, 82.8 [21.9] kg;) critically ill patients with different conditions were enrolled. SAPS II and SOFA scores were used to predict mortality in the intensive care unit. All patients were treated with colistin sulphomethate sodium (CMS) intravenously (2 M I.U.) every 8 h. After at least three days of therapy, blood samples were collected before and at 1,2,3,4,6,8 h after the end of the 30-minute IV infusion. Colistin was measured with a specific high-performance liquid chromatography method. Pharmacokinetic parameters were determined by noncompartmental analysis using the Kinetica Innaphase™ 4.0 software.

Results: Patients received 2.19 ± 0.38 mg/kg (range 1.58-2.49) of CMS per dose. At the steady-state, plasma colistin had a mean [± S.D.] AUC (0-8 h), Cthrough, Cmax, t½, CrCL of 11.54 ± 6.20 μg h/ml, 1.02 ± 0.69 μg/ml, 2.21 ± 1.08 μg/ml, 5.87 ± 2.56 h and 142.9 ± 57.8 mL/min, respectively. A clinical response was observed in 92% of patients; treatment failed in one patient with severe underlying conditions (cerebral cancer, pneumonia). The antibacterial effect of colistin was evaluated by the Cmax/MIC and AUC/MIC ratios; ratios differed according to the considered bacteria.

Conclusion: Based on our pharmacokinetic results, the maximum concentrations of colistin achieved were probably sufficient to ensure optimal Cmax/MIC ratios for all the gramnegative bacteria under study.

However, we need to redefine appropriate dosing strategies for this antibiotic in order to maximize clinical efficacy, reduce patient risk of developing bacterial resistance and minimize adverse effects.

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